

CLAIMS

1. Gene being in an isolated form and implicated in tumorigenesis having the nucleotide sequence of any one of the strands of any one of the members of the PLAG subfamily of zinc finger protein genes or CTNNB1 genes, including 5 modified versions thereof.

2. Tumorigenesis gene (T-gene) as claimed in claim 1 having at least homology with the zinc finger domains that are typical for the PLAG1 gene the nucleotide sequence of which is depicted in figure 4A, or the 10 complementary strand thereof, including modified or elongated versions of both strands.

3. T-gene as claimed in claim 1 or 2 having essentially the nucleotide sequence of the PLAG1 gene as depicted in figure 4A, or the complementary strand thereof, including 15 modified or elongated versions of both strands.

4. T-gene as claimed in claim 1 or 2 having essentially the nucleotide sequence of the PLAG2 gene as depicted in figure 8A, or the complementary strand thereof, including modified or elongated versions of both strands.

20 5. T-gene as claimed in claim 1 having essentially the nucleotide sequence of the CTNNB1 gene as depicted in figure 9, or the complementary strand thereof, including modified or elongated versions of both strands.

6. T-gene as claimed in claims 1-5 for use as a 25 starting point for designing suitable expression-modulating compounds or techniques for the treatment of non-physiological proliferation phenomena in human or animal.

7. T-gene as claimed in any one of the claims 1-6 for use as a starting point for designing suitable nucleotide probes for (clinically/medically) diagnosing cells 30 having a non-physiological proliferative capacity as compared to wildtype cells.

8. T-gene as claimed in claims 1-7, which gene is implicated in tumors selected from rhabdomyosarcoma, uterine leiomyosarcoma, uterine leiomyoma, malignant salivary gland tumors, leukemias and lymphomas. 35

9. Protein encoded by a T-gene as claimed in claims 1-8 for use as a starting point for preparing suitable antibodies for (clinically/medically) diagnosing cells having a non-physiological proliferative capacity as compared to wildtype cells.

10. Derivatives of the T-gene as claimed in claim 1-8 for use in diagnosis and the preparation of therapeutical compositions, wherein the derivatives are selected from the group consisting of sense and anti-sense cDNA or fragments thereof, transcripts of the gene or practically usable fragments thereof, fragments of the gene or its complementary strand, proteins encoded by the gene or fragments thereof, antibodies directed to the gene, the cDNA, the transcript, the protein or the fragments thereof, as well as antibody fragments.

11. In situ diagnostic method for diagnosing interphase and/or metaphase cells having a non-physiological proliferative capacity, comprising at least some of the following steps:

a) designing a set of nucleotide probes based on the information obtainable from the nucleotide sequence of the T-gene as claimed in claim 1-5, wherein at least one of the probes is hybridisable to a region of the aberrant gene substantially mapping at the same locus as a corresponding region of the wildtype gene and/or the same or another probe is hybridisable to a region of the aberrant gene mapping at a different locus than a corresponding region of the wildtype gene;

b) incubating one or more interphase or metaphase chromosomes or interphase or metaphase cells having a non-physiological proliferative capacity, with the probe(s) under hybridising conditions; and

c) visualising the hybridisation between the probe(s) and the gene.

12. Method of diagnosing cells having a non-physiological proliferative capacity, comprising at least some of the following steps:

a) taking a biopsy of a tumor to obtain cells to be diagnosed;

b) isolating a suitable T-gene-related macromolecule therefrom;

✓ 5 c) analysing the macromolecule thus obtained by comparison with a wildtype reference molecule preferably from the same individual.

13. Method as claimed in claim 12, comprising at least some of the following steps:

10 a) taking a biopsy of a tumor to obtain cells to be diagnosed;

b) extracting total RNA thereof;

c) preparing at least one first strand cDNA of the mRNA species in the total RNA extract, which cDNA comprises
15 a suitable tail;

d) performing a PCR and/or RT-PCR using a PLAG gene specific primer and a tail-specific and/or partner-specific/nested primer in order to amplify PLAG gene specific cDNA's;

20 e) separating the PCR products on a gel to obtain a pattern of bands;

f) evaluating the presence of aberrant bands by comparison to wildtype bands, preferably originating from the same individual.

25 14. Method as claimed in claim 12, comprising at least some of the following steps:

a) taking a biopsy of a tumor to obtain cells to be diagnosed;

b) isolating total protein therefrom;

30 c) separating the total protein on a gel to obtain essentially individual bands and optionally transferring the bands to a Western blot;

d) hybridising the bands thus obtained with antibodies directed against a part of the protein encoded by the
35 remaining part of the T-gene and against a part of the protein encoded by the substitution part of the T-gene;

e) visualising the antigen-antibody reactions and establishing the presence of aberrant bands by comparison

with bands from wildtype proteins, preferably originating from the same individual.

15. Method as claimed in claim 12, comprising at least some of the following steps:

- 5 a) taking a biopsy of a tumor to obtain cells to be diagnosed;
- b) isolating total DNA therefrom;
- c) digesting the DNA with one or more so-called "rare cutter" restriction enzymes;
- 10 d) separating the digest thus prepared on a gel to obtain a separation pattern;
- e) optionally transferring the separation pattern to a Southern blot;
- f) hybridising the separation pattern in the gel
- 15 or on the blot with one or more informative probes under hybridising conditions;
- g) visualising the hybridisations and establishing the presence of aberrant bands by comparison to wildtype bands, preferably originating from the same individual.

20 16. Method as claimed in any one of the claims 10-15, wherein the cells having a non-physiological proliferative capacity are selected from the group consisting of the tumors pleomorphic adenomas of the salivary gland, lipoblastomas, uterine leiomyomas, and other

25 benign tumors as well as various malignant tumors, including but not limited to sarcomas (e.g. rhabdomyosarcoma, malignant salivary gland tumors) and leukemias and lymphomas.

30 17. Anti-sense molecules of a T-gene as claimed in claims 1-8 for use in the treatment of diseases involving cells having a non-physiological proliferative capacity by modulating the expression of the gene.

18. Expression inhibitors of the T-gene as claimed in claims 1-8 for use in the treatment of diseases involving

35 cells having a non-physiological proliferative capacity.

19. Diagnostic kit for performing the method as claimed in claim 11, comprising a suitable set of labeled nucleotide probes.

